UREA AND SEROUS MEMBRANES.

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It has been known for years and has been a part of the clinical experience of all careful observers in this field, that in chronic Bright's disease, serous membranes in various parts of the body were attacked by inflammations and that these secondary conditions resulted often in the great distress or death of the individual. The pericardium became inflamed, serum accumulated and within a few hours the patient was dead. A sudden peritonitis would develop in an apparently convalescing person and the day of doom had come to the patient. An acute attack of pleurisy would set at rest another slowly tortured with the familiar dropsy, dyspnœa, and fluttering heart. Thus I might review the clinical history of many of these sufferers, and glance briefly at these inflammations in various and often remote parts of the body by way of illustration, but more than this mere mention I deem not necessary.

These inflammations at this time in the disease are doubtless due to a combination of causes, and are generally common factors with the lesion in the kidney. The waste-laden blood is carried to tissues which it has for a long period of time failed to supply with sufficient nourishment, and even the small morsel it now offers is so mixed with the offending excrementitious products that they are not able to assimilate it. The bloodvessels themselves have undergone an atheromatous degeneration that, together with the contracted arteries, causes such increase of blood-pressure that the heart has enlarged and still fails in its irregular efforts to supply the necessary nourishment. No great wonder, then, that these highly vascular and therefore most imposed upon membranes should cry out with pain and even finally succumb.

It is well known from an extended observation both of the clinical features of this disease and of the many carefully recorded tests of the excretions from the kidneys, that the excreted urea which such organs eliminate in constantly diminished quantity is, when taken with the other symptoms, the most reliable guide in diagnosis, even though the patient be passing albumin and casts. It is also known that this same relation holds good in cases not passing albumin and casts, and that the severity of the clinical features of the disease can be determined often by a knowledge of this excrementitious product, after many recorded tests have been made, without the presence of the patient.

The purpose of this paper, therefore, is to recite cases which, to my mind, make clear that serous membranes are not only involved in inflammation during the pronounced evidences of Bright's disease, but that they are often involved seriously before the times of passing albumin and casts, and that these inflammations cannot be properly considered in a diagnostic way without a thorough knowledge of the amount of urea excreted daily for a long period of time for individual cases. Finally, these cases will show that these membranes are involved in the general disturbances which are now so indefinitely known to be associated with diseased kidneys, by the common knowledge of the clinical and excreted evidence.

Pelvic Peritonitis.

Case I.—In January, 1887, I was called to see a woman in great haste on account of some acute pain in the abdomen. She was about twenty-three years of age, well nourished, married; had had no children, or abortions; no history of gonorrhœa or syphilis. For some weeks past had had slight dyspnœa on exertion, with headache. She had no other history of disease and considered herself well to this date, with exceptions noted. Physical examination showed patient in recumbent position with legs flexed on abdomen, suffering from severe pain. Pressure upon the abdomen caused increase of pain. Slight distention of bowels with gas. Examination *per vaginam* of pelvic organs disclosed great tenderness in pelvic floor, with serous effusion, most marked in front and right side of uterus. Patient, after chilly sensations, had now a temperature of 103°; pulse firm and small, beating 120 times per minute. Had slight nausea and the characteristic face. Had been attacked without traumatic or other known cause a few hours before my visit, and was now anxious to be relieved from pain. One-third of a grain of morphia was administered hypodermically and pain was allayed for several hours, after which morphia was taken by mouth to modify pain. The day following my first visit pain still continued more or less intense, unless under the influence of the anodyne. Examination *per vaginam* now disclosed more serous infiltration and consequently a more firm pelvic floor. Within a few days the characteristic "deal board" hardness and fixation of uterus was established and pain began to subside slowly, with frequent exacerbations, and terminated in recovery by slow absorption, which extended over a period of several weeks. At the close of this period patient still complained of headache, slight nausea, dyspnœa on exertion and general weakness, although she had apparently recovered her former health. Examination of her urine at this time showed no albumin or casts, after repeated trials, but the quantity of urea excreted in twenty-four hours ranged from twelve to eighteen grammes within this interval, and patient again, after six months from first attack, and soon after these examinations, lapsed suddenly into her former condition of pain and serous effusion. It now occurred to me that there was an intimate relation between the diminished quantity of urea excreted and this inflammation, as other parts of the history were negative, and in addition to the hypodermic injection of morphia I gave a second hypodermic of pilocarpine, which caused free perspiration, and this was followed by an active saline cathartic, which was repeated within twenty-four hours, and the bowels were thoroughly emptied. After three days of this kind of treatment hostilities on the part of the peritoneum had ceased, and what promised to be a more serious attack than before, terminated thus abruptly. After this experience it was determined to try, as far as possible, to avert another attack by giving attention in the interval to the excretions. Nitro-glycerin, saline cathartics, and sudorifics were vigorously used until the normal standard of from twenty-five to thirty-five grammes of urea was excreted daily and the patient so far recovered her health as to claim to be entirely well. At this time she became pregnant, and during the whole of her pregnancy she protested herself well; although I repeatedly inquired concerning her health and warned her of her probable troubles at delivery, she did not feel that she had any distress that she could not easily attribute to her condition. At about the eighth month of gestation I was called to her confinement, and after three hours of fruitless efforts, while the os was yet but slightly dilated, she had the first convulsion and continued unconscious until the child was delivered, having three other convulsions in the interim. At this time the urine showed no albumin or casts, but only 9.6 grammes of urea within twenty-four hours were excreted. Patient recovered rapidly on saline cathartics and former remedies, and since that time, May, 1889, has had but one or two slight attacks of peritoneal pain, and is well, so far as appearance and urinary tests can discover, except having a mitral regurgitant murmur, developed at or near the time of confinement, with slight enlargement of the left side of the heart. As repeated examinations of the chest were made before that time, I know the date of its appearance, and it may be well to state that no history of rheumatism can be obtained.

CASE II.—Mrs. B., aged forty, married, had had five children, no abortions. Had no history of gonorrhœa or syphilis. Had had several attacks of what a physician had called "bad misplacement of the womb," accompanied with very severe pain, before my visit. Attacks extended over several months; she was hardly up until another seizure. Before this visit had not had an attack for a month or six weeks and was in a fair state of general health. Now she had excruciating pain in region of pelvis, with knees flexed against abdomen, with increased pulse and elevated temperature. Examination *per vaginam* revealed a very tender pelvic floor with slight serous effusion on right side of uterus, which advanced from day to day, producing general hardness. As all other causes for this condition were absent, I examined the urine, to find that patient passed only 7.2 grammes of urea in twenty-four hours. Albumin and casts were never found in her urine. In ordinary fever, following acute conditions in other parts of the body, and in cases of pelvic peritonitis from other causes, urea is increased in amount. After anodynes to relieve pain, pilocarpine, saline cathartics and diuretics were used vigorously and patient made a rapid recovery. A careful record of her examinations now shows an ebb in the urea excreted, and a renewal of her former attacks, which gradually grew lighter, until, when she removed from observation, she had not had an attack for almost a year, and was apparently well, excreting from twenty-three to thirty grammes of urea in twenty-four hours.

Two other well-marked cases have come under my observation as still further illustrating these conditions, and I no longer have any doubt of the relation of these factors. One of these cases has had repeated attacks and always at the ebb of urea excretion, promptly recovering under the treatment suggested, and thus can be prevented, for long intervals, from having even slight attacks. I do not want to be considered as saying that any considerable part of the whole number of cases of pelvic peritonitis is due to this cause, but I do mean to say that such cases are frequently enough met with, even in a limited private practice, to cause a very serious reflection on the part of the profession.

PERICARDITIS.

CASE III.—In August, 1889, I was called to a man, twenty-six years of age, who was found unconscious in a water closet the previous day; had been seen by other doctors and pronounced a case of morphia poisoning. Patient was of good habits, and had no history of syphilis, rheumatism, or indeed any disease, except a profuse diarrhœa for a day or two previous, for which morphia had been taken. Examination now showed patient to be profoundly unconscious, pupils slightly dilated, pulse 110, respiration 20, slight twitching of muscles in forearm, temperature 100°. Examination of urine showed no albumin or casts, but patient passed only 9.6 grammes of urea in twenty-four hours. Saline cathartics and diuretics soon caused patient to rally, and when otherwise apparently well he still complained of the usual dyspnœa, vertigo, nausea and insomnia at times, and a record of his excretions showed at such times a very small quantity of urea excreted. At no time did he pass albumin or casts, although very frequent examinations were made. Patient was a candymaker, and went to work at his trade, against advice, in a neighboring town in last November. In January of this year he returned to the office again, suffering from what he called a bad cold, which was really another explosion of disease. Records show at this time ten grammes of urea, dyspnœa, vertigo, vomiting, twitching of muscles over body, and within two days pericardium began to fill with fluid, heart beat muffled and 110 times per minute, temperature 101°, respiration 26, dizzy and soon became unconscious, and within the night died. Post-mortem showed chronic interstitial nephritis and pericarditis with extensive effusion.

CASE IV.—This was a man, sixty-five years of age, well nourished; no history of syphilis or rheumatism; had considered himself well until within a few weeks of this consultation. Had had within this time dyspnœa, exhaustion on slight exertion, dizziness, and nausea. Had, at this first visit, a temperature of 102°, pulse 100, which had been preceded by a slight chill. Had slight distress in chest, accompanied by dyspnœa. Examination of the chest revealed an inflamed pericardium with slight effusion. The effusion during the succeeding days became very pronounced and caused quite uncomfortable dyspnœa and interfered with the heart's action. Not wishing to grant the idiopathic origin of this disease in this case and not finding another alternative, I, remembering Case I., examined his urine, to find no albumin or casts but that he passed only eight or ten grammes of urea in twenty-four hours, and that this condition extended over several days, contrary to the rule in idiopathic cases, which pass large quantities of urea. Indeed this case had almost fallen into obscurity by simulating to belong to such a class. Two other attacks followed this one within the following year and were marked by small quantities of excreted urea. The first of these was lighter than the original, and the last was lightest of all. The treatment from the beginning was nitro-glycerin, diuretics, saline cathartics, and sudorifics. The vertigo, general weakness, nausea, and dyspnœa that at first distressed patient during the intervals, gradually subsided, as excretions improved, until patient now considers himself well, as he has not had an attack of pericarditis for almost two years and the other symptoms are almost entirely relieved.

Two other well-marked cases of this variety have come under my care with similar results.

ARTHRITIS.

The relation between serous and synovial membranes is so close that I relate two cases of extensive inflammatory conditions in these membranes, as I believe them to be connected with this subject:

CASE V.—A man, twenty-one years of age; had no history of rheumatism in parents; had not had syphilis, gonorrhœa, or any serious illness until four years ago, when the present sickness began; had no bad habits—neither drank nor chewed; married, had healthy child. Had always been a farmer in easy circumstances. Four years ago had an attack of so-called rheumatism, vertigo, and general malaise. Joints of lower extremities at this time were swollen and tender; could not walk for several days, and suffered at times with them. Was treated for rheumatism in a neighboring town, and after several weeks recovered. At the same time dyspnœa and the other symptoms passed off and patient resumed his occupation, occasionally relapsing into the condition of dyspnœa and other similar symptoms. Two years ago he had a similar attack to that first mentioned and it ran an analogous course; apparently recovered, with exceptions of general weakness and dyspnœa on slight exertion. Last January I was consulted and made the following record: Joints of lower extremities slightly tender, but not much swollen, and no concretions on motion. Legs were slightly œdematous between articulations, and this had been much more marked, patient thought, during former attacks. Had marked dyspnœa, dizziness, and nausea. Had insomnia and malaise. Symptoms had been increasing in severity for the past ten days, and he feared one of his former severe attacks. The history caused me to examine the urine. I found neither albumin nor casts, but he was excreting only ten grammes of urea. Heart and other organs healthy, except slight roughness of mitral valves. The treatment before mentioned several times in this paper averted what promised to be a serious attack, and after a few weeks all distressing symptoms were gone and patient considered himself entirely well. All medication for rheumatism had not relieved any of these symptoms promptly, and some remained constantly. Patient went to Nebraska to follow his calling and consequently passed out of my charge. During the summer had another attack, and, from what I can learn from the family of his symptoms, must have died from chronic disease of kidneys, accompanied with many of former symptoms.

Another well-marked case of this kind of inflammation is now under observation—a woman, aged twenty, who has not walked for more than a year. Joints are tender and slightly swollen, but the intervening tissue is much more so. There are no concretions in the joints, no thickening of ends of bones. She has the accompanying symptoms of dyspnœa, nausea, vertigo, and a feeling of general weakness, with pale lips. Muscles are not atrophied; heart, lungs, and other organs healthy. Has no history of rheumatism, syphilis, or gonorrhœa. Parents healthy. Patient has been treated for past three years for these relapsing attacks, and is now an invalid. Examination of urine shows that patient passes but twelve to fourteen grammes of urea daily. No albumin or casts or other evidence of disease of kidneys, save those noted above. Patient has been under observation but two or three weeks, and under saline cathartics, sudorifics, and diuretics, she is rapidly improving and gives promise of walking again soon, after having been confined to the house for over a year, and having been treated for rheumatism by six or seven doctors, with all the nostrums known to the profession, without avail.

ENDARTERITIS.

CASE VI.—In April, 1886, I was called to see a woman, sixty-five years of age, who for several months past had been "gradually growing worse," as she states. Had now vertigo, blindness, nausea, and general weakness; could not walk about home without great exhaustion. Had no history of either rheumatism or syphilis in herself or parents. Did not drink alcoholic beverages. Had to be in bed at times because of irritable heart and extreme dyspnœa causing much exhaustion. Had intercostal pain and headache at times. Passed at this time but 6.7 grammes of urea in twenty-four hours. On diuretics and saline cathartics patient improved in a short time and was able to do some work and be out of doors. Urea excreted in four months after first visit amounted at one time to twenty-four grammes in twenty-four hours, and patient was comfortably well. In December, 1886, she had another explosion of former symptoms, which came on suddenly, and in addition to old symptoms had delusions and hallucinations. Same treatment again seemed to improve patient, but one night she slipped from the house and drowned herself in the river which flowed near by. Post-mortem showed extensive atheromatous degeneration of bloodvessels in head and many other regions of body. Kidneys were slightly smaller than normal, but gave no more evidence of disease than other organs, and bloodvessels were not as much changed here as elsewhere.

CASE VII.—In September, 1886, I saw a woman, forty-six years of age, who had no history of rheumatism or syphilis; the mother of several healthy children; had been for several months distressed by headache, vertigo, nausea, great dyspnœa upon slight exertion, intercostal neuralgia, and general weakness. Examination of urine at this time showed no albumin or casts, but she passed only 4.1 grammes of urea in twenty-four hours. Within two months she grew apparently better. Passed 19.2 grammes of urea, but passed trace of albumin with casts. Within the year following she developed marked insanity. At this time the radial arteries were atheromatous. The heart was slightly enlarged and with an irregular effort was doing the best service it could. Patient was sent away and died, therefore no post-mortem was made; but I have no reason to doubt the diagnosis.

CASE VIII.—A man, fifty-nine years of age; had always been healthy until about a year previous to my seeing him in July, 1886. Had no history of rheumatism or syphilis. Had healthy family of children. Drank no alcoholic beverages. Had a continuous aching in lumbar and intercostal regions, together with occasional nausea, vomiting, dyspnœa, and vertigo, which had continued for several months with varying severity. Had atheromatous condition of radial and temporal arteries. Passed from 12.7 to 15.2 grammes of urea in twenty-four hours for several weeks. Appetite generally good. After several months in this condition he had a sudden paralysis of left side, and after some months more without relief from symptoms he had another stroke, from which he finally died. No post-mortem, but no question remains of the generally diseased condition of bloodvessels.

Three or four other cases with similar histories are upon my records of the past six or seven years, and I have no doubt of the pathological changes underlying these clinical pictures, nor have I grave doubts of the steps leading up to this final fatal conclusion.

Case IX.—A clergyman, sixty-eight years of age; always an active man; never had any constitutional disease but this. Has always maintained the dignity of his profession, and is the father of several healthy children. About one year ago he began to be dizzy. Had slight dyspnœa on exertion. Has now irregular heart action. Sometimes it beats only forty times per minute for several days in succession, and quite irregularly even then. Has hardened radial arteries, slight vertigo, and insomnia. Passes only twelve to eighteen grains of urea in twenty-four hours. Passes no albumin or casts, and careful physical examination reveals to my mind no other diseased organs or tissues.

This man is still under my care. What can I tell him and his friends will finally befall him? Will he die of apoplexy, Bright's disease, endarteritis, or a combination of these, if no other disease intervene? He evidently is now at the point where all these roads meet, and it is still an open question on which one the fell destroyer will most rapidly make his approach, after he has been retarded as long as possible by the use of drugs. What shall I name this hydra-headed disease? Meigs styles it endarteritis. If in a short time he passes albumin and casts, in accordance with what Bright said many years ago, all practitioners now would unite in calling it Bright's disease. If he die from pericarditis, pleurisy, or peritonitis, without passing albumin or casts, they could not be called secondary to a primary Bright's disease; nor with this general evidence, together with the excreted evidences of ill-health, could we say that these diseases were idiopathic. We therefore need a new name that shall cover these symptoms of disease. We have abandoned dyspnœa, vertigo, and dropsy in our list of diseases, and have placed our outposts but a little further into the darkness which surrounds this whole subject, and now the facts that are brought to light from beyond these distant landmarks are demanding new names for the newly discovered conditions that shall take into account the full connotation of the term. During the time of Bright there were vaguely grouped several acute and chronic affections of the kidneys, which had in common one important characteristic—that the urine contained albumin. Almost every year since that time changes have been made in the classification to more nearly correspond to the pathological conditions, until it was discovered that patients could have otherwise this identical disease without passing albumin, and finally even albumin is beginning to be lost sight of in our rapid march toward the source of all these symptoms.

In endeavoring to find the first departure from health in the direction of these extensive after-changes in vessels, organs, and tissues, many theories have been advanced, and are of importance only so far as they can be incorporated into the clinical conditions of these patients.

George Johnson believes that chronic Bright's disease is a constitutional malady, as shown by a morbid condition of the blood, which causes changes in the secreting cells of the kidney, and then finally to changes in bloodvessels in kidneys and other organs. DaCosta and Longstreth believe that there are lesions of the renal nerve plexuses and possibly in other ganglia that should lead finally to these extensive changes in the kidneys. Semmola believes it to be a morbid change in nutrition, and that the kidney changes are due to a constant excretion of albumin. Gull and Dutton believe these extensive changes to be due, as a primary factor, to a fibrosis of the arteries and capillaries. Meigs has made perhaps the most lasting guess by first basing it upon a most worthy study of numerous pathological specimens of arteries from the different classes of these patients, and he inclines to the belief that the initial step is an endarteritis of many or few of the bloodvessels, which in the beginning or after a longer or shorter time may, and probably will, involve the arteries of the kidneys. Thomas believes that some irritating substances in the blood, as alcohol, large quantities of phosphates, urates or uric acid, lead, and oxalates, have a tendency, after a long time, to produce the contracted kidney.

If, now, anyone who has made a careful study of this whole subject, with ample clinical advantages and without bias, should be called upon to decide from these views and many others which might have been named, I am inclined to the belief that no decision could be reached as to who was most nearly in accord with all the observed phenomena of these diseases. The want of a constant sign that would be unvarying in its relation to the clinical evidence on the one hand, and the pathological changes on the other, seems to me to be much more important. It is with this object in view that I have tried to show the intimate relation which seems to exist, under all these varying conditions of this many-sided disease, between the abnormally small amount of urea excreted and these serous inflammations which precede, accompany, and follow Bright's disease. If I should be led to express a purely fanciful notion of this relation, I should be compelled to say, for want of a more plausible explanation, that urea is in some way the cause of these inflammations, or, the cause of the suppression of this excrementitious product causes such inflammations. I am inclined to this view, as the same clinical evidence exists in the patient in a more mild form, but still pronounced, as is well known to exist in some of its forms in toxic conditions resulting from an undeniable uræmia, and because at the other extreme we find this clinical evidence in very close relation to the excreted evidence before any visible sign of inflammation has begun, and are enabled to follow these patients until the first serous invasion has taken place in an apparently healthy, well-nourished, young patient oftentimes, as shown by my tables published in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1890.